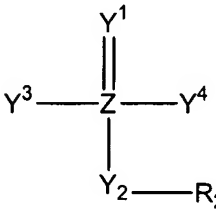
heteroatoms such as oxygen, nitrogen, sulfur or halogens (especially fluorine) possessing two or more lone electron pairs (i.e., full or partial negative charge) or electropositive hydrogen atoms (i.e., protonated amine) for hydrogen bonding with water. These include groups such as sulfone, ether, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate and acetals. Preferred groups include those which possess one or more partial or full negative charges in aqueous solution at physiological pH wherein the negatively charged atoms cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the IEM. Examples of these preferred BHEMs include negatively charged groups such as phosphate mono-ester, phosphate diester, carboxylate, and sulphonate. More preferred are those which have phosphate groups or any ester forms thereof. Even more preferred are phosphate diesters, since: a) they are highly hydrophilic with four hydrogen-bonding oxygens; b) they are relatively readily synthesized using techniques shown below; c) they serve as excellent linkers between the IEM and the PPBM; and d) because phosphate compounds exist and are metabolized naturally in the body, phosphate diester-containing contrast agents are expected to be non-toxic. --

Please replace the paragraph beginning at page 28, line 14 with the following paragraph:

-- If the moieties of this invention are positioned in the contrast agent as in structure (1) above, the BHEM is preferably sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals and more preferably



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

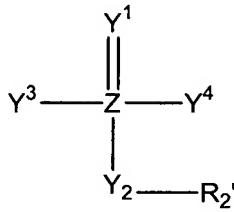
Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present. --

Most preferably, the BHEM is a phosphate group.

Please replace the paragraph beginning at page 28, line 37 with the following paragraph:

-- If the moieties of this invention are positioned in the contrast agent as in structure (2) above, the BHEM is preferably sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals and more preferably the BHEM has the following formula:



or ester forms,

where Z = P, W, or Mo

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present.

Most preferably, the BHEM is a phosphate group. --

Please replace the paragraph beginning at page 29, line 19 with the following paragraph:

--If the moieties of this invention are positioned in the contrast agent as in structure (3) above, the BHEM is preferably SO_3^- or ester forms, sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetal and more preferably

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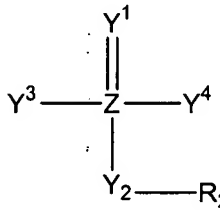

or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present.

Most preferably, the BHEM is a phosphate group. --

Please replace the paragraph beginning at page 31, line 14 with the following paragraph:

A6

-- For contrast agents comprising the formulas shown above, the metal ion M is more preferably Gd(III), Fe(III), Mn(II), Mn(III), Cr(III), Cu(III), Dy(III), Tb(III), Ho(III), Er(III) or Eu(III), and most preferably Gd(III). The BHEM is preferably sulfone, ether, urea, thio-urea, amine, amide, sulfonamide, carbamate, peptide, ester, carbonate, acetal and more preferably COO^- or ester forms, SO_3^- or ester forms and

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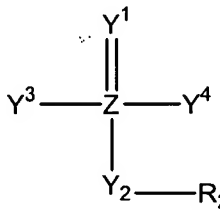

or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present. --